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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,357	11/24/2003	Michela Gallagher	JHUC-0008-101	4705

1473 7590 02/08/2008

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PATENT DOCKETING 39/361
1211 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-8704

EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
02/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/722,357	GALLAGHER ET AL.	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/21/07; 11/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, received 11/5/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Applicant's claim amendment, received 11/5/07, is acknowledged and entered of record. Applicant's statement that the claim amendments are fully supported by the specification and that no new matter has been introduced is acknowledged. Applicant's statement that support for the amendment to claim 44 can be found, for example, in claim 38 as originally filed, at page 86, last two paragraphs, and at page 83, lines 5-6, is acknowledged and made of record.

It is noted that the term *"attenuating the effects of age-associated cognitive impairment in a mammal"* as recited in instant claim 44 is not found to be expressly disclosed in the original claim 38 or at page 83, or page 86. However, given its broadest reasonable possible interpretation this term is construed to be encompassed by the term "treatment of age-associated cognitive impairment in a mammal." Thus, no new matter is deemed to have been introduced by the amendment as evidenced by the instant disclosure at page 83, lines 1-5 (see also Webster's New Collegiate Dictionary. 1981, page 72).

The new rejection under 112, 2nd paragraph is necessitated by the claim amendment.

This action is final.

Status of the Claims

Claims 44 and 53 are currently pending in this application and are the subject of the Office action.

Claims 1-43, 42-52, and 54-62 are cancelled.

Request for Correction of Inventorship pursuant to CFR 1.48(b)

In view of the papers filed 11/05/07, the inventorship in this nonprovisional application has been changed by the deletion of Jeffrey D. Rothstein.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Response to applicant's arguments/remarks

Written description rejection under 112, 1st para

Applicant contends that this rejection should be withdrawn because of the following:

1) The instant disclosure satisfies the written description requirement and shows that applicants had possession of the claimed invention as evidenced by the fact descriptive means disclosed therein such as words, structures, and formulas (see MPEP 2163).

2) A skilled artisan clearly can "envision the detailed chemical structure of the encompassed derivatives, analogs, etc. based on the disclosure.

In response, although applicant's arguments are not found to be persuasive, the rejection is withdrawn as the claim amendment renders this rejection moot.

Scope of enablement rejection under 112, 1st para

Applicant contends that this rejection should be withdrawn for the following reasons:

1) The amendment of the claims to recite/encompass compounds of formula II, wherein X is OH, -O-alkali metal, -NH2, or –DH; and R is –CH[(CH2)2CH3]2, the deletion of the term "preserving cognitive function," and the replacement of the latter term with the term "attenuating the effects of age-associated cognitive impairment" renders the rejection moot.

2) The specification provides enabling disclosure to support the instant claimed invention as evidenced by the disclosure that valproic acid and related compounds can modulate expression of a gene associated with age-associated cognitive impairment (e.g. page 86).

3) The specification discloses well-known and accepted techniques for formulation and administration of compositions comprising one or more active ingredients and methods of administration and dosage information (e.g. pages 88-93).

4) Example 9.3 provides a specific working example showing the effect of ceftriaxone (not valproic acid) treatment effects on cognitive function in age-impaired

rats. However, the application also provides sufficient details that would enable one of ordinary skill in the art to practice the claimed methods with compounds other than ceftriaxone as evidenced by Koh et al. (Exhibit B i.e. reference CB listed on the IDS received 11/13/07).

5) Although the cognitive abilities of humans are more advanced and complex than rodents, those of ordinary skill in the art have long recognized that data obtained from in vitro rat models (such as the Long-Evans rat model) that reasonably correlate with pharmacological effects in humans as evidenced by Gallagher et al. (Exhibit A i.e. reference CA listed on IDS received 11/13/07; see also instant specification page 2, last para.)

In response, this rejection is withdrawn in view of applicant's persuasive arguments and claim amendments.

Rejection under 102(e)

Applicant contends that this rejection should be withdrawn for the following reasons:

1) Ohuchida et al. refer only generally to improving brain functions and to improving cerebral function (col. 1, line 28; col. 2, lines 9-19; col. 3, lines 55-60; col. 5, lines 37-43; col. 27, lines 66-67; col. 31, lines 22-23), but never refer to improving cognitive function or attenuating the effects of age-associated cognitive impairment. Although Ohuchida et al. teach "improving functional activities of astrocytes and improving $GABA_A$ receptor responses are expected to be useful for neurodegenerativer

diseases," they do not teach the claimed limitation of "attenuating the effects of age-associated cognitive impairment on cognitive function."

2) Ohuchida et al. studied astrocyte function and $GABA_A$ receptor response using young rats (cerebrum of neonatal rats at the age of 1 day), which do not constitute rats with age-associated cognitive impairment. Thus, Ohuchida et al used a test that would not have measured the effect claimed in this application. Furthermore, other studies confirm that valproic acid and its salts have an adverse effect on cognitive function, learning and memory, in young [sic] rats as evidenced by Wu et al. (Exhibit C i.e. reference CC of IDS received 11/13/07).

In response, the rejection is maintained for the following reasons:

a) The term "attenuating the effects of age-associated cognitive impairment on cognitive function," as recited in claim 44, given its broadest reasonable possible interpretation is construed to be the functional equivalent of "treating age-associated cognitive impairment" as evidenced the dictionary definition of the term "attenuate" (See Webster's New Collegiate Dictionary. 1981, page 72).

b) Ohuchida et al. teach a method for treatment of neurodegenerative diseases, (including Alzheimer's disease) comprising administering pentanoic acid derivatives, including valproic acid, in amounts useful for treating said diseases (see abstract). To the extent that the instant claimed method encompassses the treatment of diseases, including Alzheimer's disease, comprising administering therapeutic amounts of compounds having the general formula recited II as recited in claim 44 (including valproic acid as a compound species (i.e. X = OH, R = CH[(CH2)2CH3]2), as the only

active method step, the instant claims are found to be anticipated by the prior art, as further evidenced by Wu et al. The effects of antiepileptic drugs on spatial learning and hippocampal protein kinase C γ in immature rats. Brain & Development. 2002, 24: 82-87; already made of record by applicant; see also instant specification, e.g. page 1, 3rd para.).

Wu et al. teach that epilepsy is a chronic disease requiring long-term therapy with antiepileptic drugs such as valproic acid and that children with epilepsy have a higher incidence of impaired cognitive function (page 82, first para.; and page 85).

Rejections

Claim rejection under 102(e)

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 44 and 53 are anticipated by Ohuchida et al (US Patent 7, 176, 240 B2).

The above discussion in connection with the Response to applicant's arguments/remarks to the 102(e) rejection in incorporated by reference.

Ohuchida et al. (US Patent 7,176,240 B2) teach pentanoic acid derivatives are potentially useful in improving the GABAa receptor responses (column 3, lines 53-61; columns 7-8). Ohuchida et al teach, for example, 2-propylpentanoic acid, known as valproic acid, and 2-propylpentanamide, which is also known as valpromide; both

agents are antiepileptic drugs (column 3, line 66 to column 4, line 38). Formula II of the instant application also overlaps other pentanoic acid derivatives taught by Ohuchida et al. e.g. 2-ethylhexanoic acid, 2-propylhexanoic acid, 2-propyldecanoic acid (column 3, line 67 to column 4, line 67). Ohuchida et al. also teach that these pentanoic acid derivatives and non-toxic salts and acid addition salts thereof are useful for prevention and/or treatment for neurodegenerative disease (Alzheimer's disease etc.) and neuronal dysfunction by stroke or traumatic injury (multiple sclerosis etc.) (abstract). Ohuchioda et al. disclose that abnormalities in the astrocyte may be the determinant factors in inducing various brain-related diseases (column 2, lines 17-19). In view of applicant's disclosure that there are many conditions, such as dementias (e.g. Lewy body dementia, vascular dementia, Alzheimer's Diseases, and HIV associated dementia), Huntington's Disease, Parkinson's Disease, schizophrenia, depression, amyotrophic lateral sclerosis, Mild Cognitive Impairment (MCI) and Age Related Cognitive Decline (ARVD), of which sensitive detection of cognitive impairment would benefit the sufferer of the condition, the instant application and the reference overlap with respect to the treatment groups and the actual treatment using pentanoic acid derivatives. Thus, the instant claims are anticipated by Ohuchida et al.

Newly applied rejection under 112, 2nd para

Claim rejections – 35 USC 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 recites the below term "comprising the step of administering a pharmaceutical composition comprising a therapeutically effective amount of:

II

to said mammal, wherein:

X is -OH, -O-alkali metal, $-NH_2$, or $-SH$; and

R is $-CH[(CH_2)_2CH_3]_2$.

However, the term below term represented by formula II, does not specifically a specific compound as X could be OH, or -O-alkali metal, -NH2, or SH

II

It is suggested that this rejection may be overcome by amending the claim to recite the term "a compound having the below formula" immediately following the word "of" but before the punctuation mark ":" as recited in claim 44 provided the amendment is supported by the specification as originally filed.

Claim 53 is also found to be vague and indefinite for failing to refer back to a specific claim even though it recites the term "[T]he method of claim ..." It is suggested that this rejection may be overcome by amending the claim to recite the term "44" immediately following the term "claim."

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

27 January 2008
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER